AMENDMENTS TO THE CLAIMS:

Please amend claims 29, 68, 81, 72 and 89-91 as follows. This listing of claims replaces all prior versions, and listings of claims, in the application.

LISTING OF CLAIMS:

1-25. (Cancelled)

26. **(Previously Presented)** The method of claim 29, wherein the immune effector cells are leukocytes that express chemokine receptors.

27. **(Previously Presented)** The method of claim 29, wherein the inflammatory response results in secondary tissue damage.

28. **(Previously Presented)** The method of claim 29, wherein the immune effector cells are selected from mononuclear phagocytes (MNP), leukocytes, natural killer cells, dendritic cells, T lymphocytes and B lymphocytes.

29. **(Currently Amended)** A method for inhibiting ~~activation,~~ proliferation or migration of <u>activated</u> immune effector cells, comprising administering a conjugate to an animal, whereby ~~activation,~~ proliferation or migration of the immune effector cells is inhibited, wherein:

the conjugate comprises a targeted agent or a portion thereof and a chemokine receptor targeting agent or a portion thereof sufficient to bind to a chemokine receptor on immune effector cells and facilitate internalization of the conjugate;

the chemokine receptor targeting agent is a chemokine, an antibody that specifically binds to a chemokine receptor or a fragment of the chemokine or antibody, wherein the chemokine, antibody or fragment thereof binds to the receptor and internalizes the targeted agent in a cell;

the targeted agent or portion thereof, when internalized in a cell, alters metabolism or gene expression in the cell, regulates or alters protein synthesis in the cell, inhibits proliferation of the cell or kills the cell; and

the conjugate binds to a chemokine receptor resulting in internalization of the targeted agent in cells bearing the receptor.

30. (Cancelled)

31. **(Previously Presented)** The method of claims 29, wherein the activated, proliferating or migrating immune cells occur in a disorder or disease state that is selected from the group consisting of CNS injury, CNS inflammatory diseases, neurodegenerative disorders, heart disease, inflammatory eye diseases, inflammatory bowel diseases,

inflammatory joint diseases, inflammatory kidney or renal diseases, inflammatory lung diseases, inflammatory nasal diseases, inflammatory thyroid diseases, inflammatory responses associated with bacterial or viral infections and cytokine-regulated cancers.

32. **(Original)** The method of claim 31, wherein the CNS inflammatory diseases and neurodegenerative disorders are selected from the group consisting of stroke, closed head injury, leukoencephalopathy, choriomeningitis, meningitis, adrenoleukodystrophy, AIDS dementia complex, Alzheimer's disease, Down's Syndrome, chronic fatigue syndrome, encephalitis, encephalomyelitis, spongiform encephalopathies, multiple sclerosis, Parkinson's disease, and spinal cord injury/trauma (SCI).

33. (Cancelled)

34. **(Previously Presented)** The method of claim 29, wherein the targeted agent is a toxin.

35. **(Previously Presented)** A method of targeted delivery of an agent into cells that express chemokine receptors, comprising associating the agent with a chemokine receptor targeting agent, whereby:

the chemokine receptor targeting agent binds to a chemokine receptor expressed on the cells; and

the agent is internalized by the cells, wherein the cells are immune effector cells.

36. **(Previously Presented)** The method of claim 35, wherein the immune effector cells are activated leukocytes.

37. **(Original)** The method of claim 27, wherein the secondary tissue damage results from spinal cord injury or trauma.

38-39. (Cancelled)

40. **(Previously Presented)** A method for inhibiting the proliferation, migration or activity of secondary tissue damage-promoting inflammatory cells, comprising administering to a subject in need thereof an effective amount of a therapeutic agent that inhibits the proliferation, migration or physiological activity of secondary tissue damage-promoting inflammatory cells, wherein the therapeutic agent is a conjugate that comprises a chemokine receptor targeting agent and a targeted agent or portion thereof selected so that conjugate binds to a chemokine receptor and internalizes the targeted agent, which inhibits the proliferation, migration or physiological activity of the secondary tissue damage-promoting cells.

41. (Cancelled)

42. **(Previously Presented)** The method of claim 29, wherein the conjugate is selected from the group consisting of OPL98104, OPL98112, OPL98108, OPL98102, OPL98110, OPL98106, OPL98101, OPL98109, OPL98105, OPL98103, OPL98111 and OPL98107.

43. (Cancelled)

44. **(Previously Presented)** The method of claim 29, wherein the conjugate comprises the following components: (chemokine receptor targeting agent)n, (L)q and (targeted agent)m, wherein:

L is a linker for linking the chemokine receptor targeting agent to a targeted agent;

chemokine receptor targeting agent is any moiety that selectively binds to a chemokine receptor and effects internalization of the conjugate;

m and n, which are selected independently, are at least 1; and

q is 0 or more as long as the resulting conjugate binds to the targeted receptor, is internalized and delivers the targeted agent;

the resulting conjugate binds to a receptor that interacts with and internalizes a chemokine, whereby the targeted agent(s) is internalized in a cell bearing the receptor; and

when the conjugate contains a plurality of targeted agents, the targeted agents are the same or different, and when the conjugate contains a plurality of chemokine receptor targeting agents, the targeting agents are the same or different.

45. **(Previously Presented)** The method of claim 44, wherein m and n, which are selected independently, are 1-6.

46. **(Previously Presented)** The method of claim 44, wherein q is 1, n is 2 and m is 1.

47. (Cancelled)

48. **(Previously Presented)** The method of claim 44, wherein the chemokine receptor targeting agent specifically binds to chemokine receptors on activated leukocytes.

49. **(Previously Presented)** The method of claim 44, wherein the chemokine receptor targeting agent specifically binds to chemokine receptors on activated cells selected from mononuclear phagocytes (MNP), leukocytes, natural killer cells, dendritic cells, T lymphocytes and B lymphocytes.

50. **(Previously Presented)** The method of claim 49, wherein the activated leukocytes are selected from basophils, neutrophils, eosinophils or combinations of any two or more thereof.

51. **(Previously Presented)** The method of claim 44, wherein the targeted agent is a toxin, a nucleic acid or a therapeutic protein.

52. **(Previously Presented)** The method of claim 44, wherein the chemokine receptor targeting agent and targeted agent are linked directly via a covalent or ionic linkage.

53. **(Previously Presented)** The method of claim 44, wherein the chemokine receptor targeting agent and targeted agent are joined via a linker.

54. **(Previously Presented)** The method of claim 53, wherein the linker is a peptide linkage, a polypeptide or is chemical linker.

55-56. (Cancelled)

57. **(Previously Presented)** The method of claim 44, wherein the chemokine receptor targeting agent is a chemokine or a fragment thereof that binds to the receptor and internalizes the targeted agent.

58-64. (Cancelled)

65. **(Previously Presented)** The method of claim 29, wherein the chemokine receptor targeting agent is a chemokine or a sufficient portion thereof to specifically bind to a chemokine receptor and to facilitate internalization of the conjugate.

66. **(Previously Presented)** The method of claim 29, wherein the chemokine targeting agent is a chemokine that is a member of the superfamily of chemokines that interact with at least one of the chemokine receptors selected from the group consisting of the CC-, CXC-, CX3C- and XC-receptors.

67. **(Previously Presented)** The method of claim 29, wherein the chemokine targeting agent is a chemokine that is a member of the superfamily of chemokines that interact with at least one of the chemokine receptors selected from the group consisting of the CC- and CXC- receptors.

68. **(Currently Amended))** The method of claim 65, wherein the chemokine is selected from the group consisting of IL-8, GCP-2, GRO-α, GRO-β, GRP-γ, ENA-78, PBP, CTAP III, NAP-2, LAPF-4, MIG, ~~PF4,~~ IP-10, SDF-1α, SDF-1β, SDF-2, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, MIP-1α, MIP-1β, MIP-1γ, MIP-2, MIP-2α, MIP-3α, MIP-3β, MIP-4, MIP-5, MDC, HCC-1, LD78β, eotaxin-1, eotaxin-2, I-309, SCYA17, TARC, RANTES, DC-CK-1, lymphotactin and fractalkine.

69. **(Previously Presented)** The method of claim 65, wherein the chemokine is selected from the group consisting of lungkine, ALP, Tim-1, chemokine α-5, chemokine α-6 and chemokine β15.

70. **(Previously Presented)** The method of claim 29, wherein the chemokine receptor selected from the group consisting of CXCR-1, CXCR-2, CXCR-3, CXCR-4, CXCR-5, CCR-1, CCR-2A, CCR-2B, CCR-3, CCR-4, CCR-5, CCR-6, CCR-7, CCR-8, CCR-8, CX3CR-1, XCR1, Duffy antigen receptor for chemokines (DARC) and CD97.

71. **(Previously Presented)** The method of claim 65, wherein the chemokine receptor is selected from the group consisting of DARC, CXCR-1, CXCR-2, CXCR-3, CXCR-4, CCR-1, CCR-2A, CCR-2B, CCR-3, CCR-4, CCR-5, CCR-6, CCR-7, CCR-8, CX3CR-1, and CD97.

72. **(Currently Amended)** A method for inhibiting ~~activation,~~ proliferation or migration of <u>activated</u> immune <u>effector</u> cells, comprising contacting immune <u>effector</u> cells with a conjugate that comprises a targeted agent or a portion thereof and a chemokine receptor targeting agent, whereby activation~~,~~ <u>or</u> proliferation~~, migration~~ of the immune <u>effector</u> cells is inhibited, wherein:

the targeted agent or portion thereof is a toxin;

the chemokine receptor targeting agent is a chemokine or a fragment of thereof that binds to a chemokine receptor and internalizes the targeted agent; and

the conjugate binds to a chemokine receptor resulting in internalization of the targeted agent in cells bearing the receptor.

73. **(Previously Presented)** The method of claim 72, wherein the conjugate comprises the following components: (chemokine receptor targeting agent)n, (L)q and (targeted agent)m, wherein:

L is a linker for linking the chemokine or fragment thereof to a targeted agent;

m and n, which are selected independently, are at least 1; and

q is 0 or more as long as the resulting conjugate binds to the targeted receptor, is internalized and delivers the targeted agent;

the resulting conjugate binds to a receptor that interacts with and internalizes a chemokine, whereby the targeted agent(s) is internalized in a cell bearing the receptor; and

when the conjugate contains a plurality of targeted agents, the targeted agents are the same or different, and when the conjugate contains a plurality of chemokine receptor targeting agents, the targeting agents are the same or different.

74. **(Previously Presented)** The method of claim 73, wherein m and n, which are selected independently, are 1-6.

75. **(Previously Presented)** The method of claim 73, wherein q is 1, n is 2 and m is 1.

76. **(Previously Presented)** The method of claim 73, wherein the chemokine specifically binds to chemokine receptors on activated leukocytes.

77. **(Previously Presented)** The method of claim 73, wherein the chemokine specifically binds to chemokine receptors on activated cells selected from mononuclear phagocytes (MNP), leukocytes, natural killer cells, dendritic cells, T lymphocytes and B lymphocytes.

78. **(Previously Presented)** The method of claim 76, wherein the activated leukocytes are selected from basophils, neutrophils, eosinophils or combinations of any two or more thereof.

79. **(Previously Presented)** The method of claim 73, wherein the chemokine is a member of the superfamily of chemokines that interact with at least one of the chemokine receptors selected from the group consisting of the CC-, CXC-, CX3C- and XC-receptors.

80. **(Previously Presented)** The method of claim 73, wherein the chemokine is a chemokine that is a member of the superfamily of chemokines that interact with at least one of the chemokine receptors selected from the group consisting of the CC- and CXC-receptors.

81. **(Currently Amended)** The method of claim 35, wherein the chemokine is selected from the group consisting of IL-8, GCP-2, GRO-α, GRO-β, GRP-γ, ENA-78, PBP, CTAP III, NAP-2, LAPF-4, MIG, ~~PF4~~, IP-10, SDF-1α, SDF-1β, SDF-2, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, MIP-1α, MIP-1β, MIP-1γ, MIP-2, MIP-2α, MIP-3α, MIP-3β, MIP-4, MIP-5, MDC, HCC-1, LD78β, eotaxin-1, eotaxin-2, I-309, SCYA17, TARC, RANTES, DC-CK-1, lymphotactin, and fractalkine.

82. **(Previously Presented)** The method of claim 40, wherein the targeted agent, when internalized in a cell, alters metabolism or gene expression in the cell, regulates or alters protein synthesis in the cell, inhibits proliferation of the cell or kills the cell.

83. **(Previously Presented)** The method of claim 29, wherein the targeted agent is selected from among ribosome inactivating proteins (RIPs) and bacteriocins.

84. **(Previously Presented)** The method of claim 73, wherein the toxin is a ribosome inactivating protein or a toxic subunit thereof.

85. **(Previously Presented)** The method of claim 29, wherein the targeted agent is a toxin that is a ribosome inactivating protein or a toxic subunit thereof.

86. **(Previously Presented)** A method of preparing a candidate compound for treating a disease or disorder involving activated immune cells an inflammatory response, comprising:

identifying immune cells that are activated in the disease or disorder;

identifying chemokine receptors expressed on the cells;

preparing a conjugate or plurality thereof containing toxin linked to a chemokine or a plurality of chemokines that specifically bind to the identified chemokine receptors and effect or facilitate internalization of the toxin into the cells.

87. **(Previously Presented)** The method of claim 86, wherein a plurality of conjugates that bind to a plurality of chemokine receptors are prepared.

88. **(Previously Presented)** The method of claim 29, wherein the chemokine receptor targeting agent is selected from the group consisting of IL-8, GRO-α, GRO-β, IP-10, SDF-1β, MCP-1 MCP-3, eotaxin-1, eotaxin-2 and RANTES.

89. **(Currently Amended)** The method of claim 57, wherein the chemokine receptor targeting agent is selected from the group consisting of IL-8, GCP-2, GRO-α, GRO-β, GRP-γ, ENA-78, PBP, CTAP III, NAP-2, LAPF-4, MIG, ~~PF4~~, IP-10, SDF-1α, SDF-1β, SDF-2, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, MIP-1α, MIP-1β, MIP-1γ, MIP-2, MIP-2α, MIP-3α, MIP-3β, MIP-4, MIP-5, MDC, HCC-1, LD78β, eotaxin-1, eotaxin-2, I-309, SCYA17, TARC, RANTES, DC-CK-1, lymphotactin, and fractalkine.

90. **(Currently Amended)** The method of claim 40, wherein the chemokine receptor targeting agent is selected from the group consisting of IL-8, GCP-2, GRO-α, GRO-β, GRP-γ, ENA-78, PBP, CTAP III, NAP-2, LAPF-4, MIG, ~~PF4~~, IP-10, SDF-1α, SDF-1β, SDF-2, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, MIP-1α, MIP-1β, MIP-1γ, MIP-2, MIP-2α, MIP-3α, MIP-3β, MIP-4, MIP-5, MDC, HCC-1, LD78β, eotaxin-1, eotaxin-2, I-309, SCYA17, TARC, RANTES, DC-CK-1, lymphotactin, and fractalkine.

91. **(Currently Amended)** The method of claim 86, wherein the chemokine is selected from the group consisting of IL-8, GCP-2, GRO-α, GRO-β, GRP-γ, ENA-78, PBP, CTAP III, NAP-2, LAPF-4, MIG, ~~PF4,~~ IP-10, SDF-1α, SDF-1β, SDF-2, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, MIP-1α, MIP-1β, MIP-1γ, MIP-2, MIP-2α, MIP-3α, MIP-3β, MIP-4, MIP-5, MDC, HCC-1, LD78β, eotaxin-1, eotaxin-2, I-309, SCYA17, TARC, RANTES, DC-CK-1, lymphotactin, and fractalkine.

92. **(Previously Presented)** The method of claim 29, wherein the immune effector cells are selected from among monocytes, macrophages, leukocytes and microglia.

93. **(Previously Presented)** The method of claim 44, wherein the immune effector cells are selected from among monocytes, macrophages, leukocytes and microglia.

94. **(Previously Presented)** The method of claim 35, wherein the immune effector cells are selected from mononuclear phagocytes (MNP), leukocytes, natural killer cells, dendritic cells, T lymphocytes and B lymphocytes.

95. **(Previously Presented)** The method of claim 35, wherein the immune effector cells are selected from among monocytes, macrophages, leukocytes and microglia.

96. **(Previously Presented)** The method of claim 86, further comprising:

contacting the immune cells with the conjugate or plurality thereof, whereby the toxin is internalized.

97. **(Previously Presented)** The method of claim 96, wherein a plurality of conjugates that bind to a plurality of chemokine receptors are prepared, and the immune cells are contacted with each of the conjugates simultaneously or sequentially.